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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/802,668	03/09/2001	Steven L. Roberds	PHRM-0319	3061

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EXAMINER
CHERNYSHEV, OLGA N

ART UNIT	PAPER NUMBER
1646	18

DATE MAILED: 01/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/802,668	ROBERDS ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-116* is/are pending in the application.

4a) Of the above claim(s) *1-94 and 97-116* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *95 and 96* is/are rejected.

7)☒ Claim(s) *95 and 96* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5, 9 OC 01/23/03
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group III and SEQ ID NO: 105 in Paper No. 14 is acknowledged. The traversal is on the ground(s) that the 37 groups of claims are amendable to further grouping and that such further grouping would not impose a serious burden on the Examiner. This is not found persuasive because an application may properly be required to be restricted to one of two or more claimed inventions if they are able to support separate patents and they are either independent (MPEP § 806.04 - § 806.04 (j)) or distinct (MPEP § 806.05 - § 806.05 (i)). The Examiner has shown that the Groups I-XXXVII are independent or distinct for the reasons in the previous Office action (see Paper No. 8). Furthermore, MPEP § 803 provides that the separate classification (i.e., class and subclass) of distinct inventions is sufficient to establish a *prima facie* case that the search and examination of the plural inventions would impose a serious burden upon the Examiner; such separate classification was set forth in the Office action mailed January 30, 2002 (Paper No. 8).

The requirement is still deemed proper and is therefore made FINAL.

Invention of Group III corresponds to claims 36-38 and 95-96, however, only claims 95 and 96 encompass an antibody to the elected SEQ ID NO: 105. Therefore, claims 1-94 and 97-116 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 14.

Claims 95 and 96, in so far as they are directed to an antibody that binds to a polypeptide encoded by a nucleic acid that encodes a polypeptide comprising an amino acid sequence homologous to SEQ ID NO: 105, are under examination in the instant office action.

Oath/Declaration

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
It does not identify the citizenship of inventor Roberds.

Specification

3. The text of Table 5, pages 84-102, is not in compliance with the requirements for Sequence Identifiers (see MPEP 2422.03). The appropriate format for sequence identifiers is SEQ ID NO: X, wherein "X" is the sequence number. Appropriate correction is required.

Applicant is advised to review the entire text of the instant specification for proper use of sequence identifiers.

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Antibodies to human ion channels.

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, see page 103, for example. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The use of the trademarks has been noted in this application, see page 24, for example. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Applicant is advised to review the entire text of the specification for other possible use of hyperlinks or trademarks.

Claim Objections

6. Claims 95 and 96 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 96 depends from claim 95, and claim 95 depends from claim 89, which is limited to a polynucleotide, encoded by a nucleic acid of claim 76, while claim 95 encompasses an antibody. Claim 95 is improper because it can be infringed by an antibody, which does not infringe claims 89 or 76. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Applicant should note the "Infringement Test" for dependent claims in MPEP § 608.01(n). The test for a proper dependent claim is whether the dependent claim includes every limitation of the parent claim. A proper dependent claim shall not conceivably be infringed by anything, which would not also infringe the basic claim. In the instant case, the antibody claims could be infringed without infringing the claims from which it depends, i.e. the protein and nucleic acid claims. Therefore, they are improperly dependent and should be rewritten in independent form.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 95 and 96 are rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. Because the instant application does not disclose the biological role of this protein or its significance, an antibody to the protein cannot be considered particularly useful.

It is clear from the instant application that the protein described therein is what is termed an "orphan protein" in the art. The DNA of the instant application has been isolated because of its similarity to a known DNA. There is little doubt that, after complete characterization, this DNA and encoded protein may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility. The court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion".

The instant claims are drawn to an antibody that binds to a polypeptide of as yet undetermined function or biological significance. It is asserted in the instant specification that the novel nucleic acids of the instant invention encode human ion channels, ion-x (page 1, second paragraph of the instant specification). The general role of the major types of ion channels is disclosed on pages 1-4. It is further stated that "ion channels may be useful targets for discovering ligands or drugs to treat many diverse disorders and defects, including schizophrenia, depression, anxiety, attention deficit hyperactivity disorder, migraine, stroke, ischemia, and neurodegenerative disease such as Alzheimer's disease, Parkinson's disease, glaucoma and macular degeneration. In addition compounds which modulate ion channels can be useful for the treatment of cardiovascular diseases including ischemia, congestive heart failure, arrhythmia, high blood pressure and restenosis" (page 4, third paragraph). It is clear from the instant specification that the nucleic acids of the invention were isolated because of the structural similarity to the nucleic acids encoding known human ion channels (pages 102-103). Thus, based on the structural similarities to different known proteins with well-established function, it has been suggested that the polypeptides of the instant invention would also possess similar biological activity. Numerous publications exist on a topic of predicting protein functions from structural similarities or homology to the known proteins. It is well described in the art that

amino acid structure cannot necessarily predict the function of the protein: "Knowing the protein structure by itself is insufficient to annotate a number of functional classes and is also insufficient for annotating the specific details of protein function" (see Skolnick et al., Box 2 on page 36 and the whole paper). Moreover, "Structural similarity does not necessarily mean a common evolutionary origin and homologous sequences may evolve into different folds (according to current classification schemes) (See Bork et al., Current Opinion in structural Biology, 1998, 8, page 332, first column, second paragraph). Thus, according to the state of the art, functional characteristics of a protein cannot be unequivocally extrapolated from its structural characteristics.

In the absence of knowledge of the biological significance of this specific polypeptide of SEQ ID NO: 105, there is no immediately obvious patentable use for this polypeptide and, consequently, for the antibody that binds to an epitope of the polypeptide of SEQ ID NO: 105. According to the specification of the instant application "[a]ntibodies of the invention are useful for, *e.g.*, therapeutic purposes (by modulating activity of ion-x), diagnostic purposes to detect or quantitate ion-x, and purification of ion-x" (page 52, paragraph six of the instant specification). It is also asserted that ion-x polypeptides and modulators may be used in the treatment of various diseases, disorders and pathological conditions (full list of such conditions is disclosed on pages 63 and 72 of the instant specification). However, the instant specification fails to provide any evidence or sound scientific reasoning that would support a conclusion that the instant ion-x polypeptides and a polypeptide of SEQ ID NO: 105 in particular, are associated with any particular disease or disorder. To employ an antibody, which binds to an epitope on a polypeptide homologous to a polypeptide of SEQ ID NO: 105 in the future diagnostic assays or

methods of purification of ion-x proteins is not a "real world" because it would ultimately relate to a protein for which no biological function is known. The instant application also fails to demonstrate use of the antibody as a marker for any disease or condition (which would be a real world use). Because the instant specification does not teach a biological activity of this specific polypeptide of SEQ ID NO: 105, which supports a practical utility, one would not reasonably believe that the modulation of ion-x channel of SEQ ID NO: 105 by use of the antibody that binds polypeptide of SEQ ID NO: 105 would serve any therapeutic purpose, as implied by the specification. To employ the claimed antibody of the instant invention in any of the disclosed methods would clearly be using it as the object of further research, which has been determined by the courts to be a utility, which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for the claimed antibody, then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 95 and 96 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

9. Claims 95 and 96 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 95 and 96 are directed to an antibody which binds to an epitope on a polypeptide encoded by an isolated nucleic acids molecule comprising a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence homologous to SEQ ID NO: 105. Because of the use of "comprising" language in the preceding claims, the instant claims encompass virtually every antibody in existence. There is no recitation in the claims 95 or 96 that would limit the claimed subject matter to an antibody related only to a polypeptide of SEQ ID NO: 105. The instant specification fails to describe the entire genus of antibodies, which are encompassed by these claims. In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant has possession of a nucleic acid molecule which encodes a protein which has the amino acid sequence of SEQ ID NO: 105 and an antibody that binds to an epitope confined within this particular sequence. However, the claims are not limited to an antibody that binds to an epitope within an amino acid sequence of SEQ ID NO: 105 but encompass an antibody that binds to any epitope that can be outside of SEQ ID NO: 105. The instant specifications only describes an antibody that binds to an epitope of a protein having the amino acid sequence of SEQ ID NO: 105 and fails to teach or describe any other antibody that binds to a protein which lacks the amino acid sequence of SEQ ID NO: 105. Therefore, there is a lack of guidance or

teaching regarding structure and function because there is only a single example provided in the specification and because there is no guidance found in the prior art.

Next in making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, each claimed species and genus must be evaluated to determine whether there is sufficient written description to inform a skilled artisan that applicant was in possession of the claimed invention at the time the application was filed. With this regard, the instant application fails to provide a written description of the species or the entire genus which are encompassed by the instant claims except for the antibody that binds to an epitope within an amino acid sequence of SEQ ID NO: 105. The claims also fail to recite other relevant identifying characteristics (physical and/or chemical and/or functional characteristics coupled with a known or disclosed correlation between function and structure) sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. Because the claims, as written, encompass basically every known antibody as well as those yet to be discovered, a conclusion can be made that the claims are directed subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 95 and 96 are rejected under 35 U.S.C. 102(b) as being anticipated by Hopp et al., US Patent No. 5,011,912, 1991.

Claims 95 and 96 are directed to an antibody which binds to an epitope on a polypeptide encoded by an isolated nucleic acids molecule comprising a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence homologous to SEQ ID NO: 105. Because of the use of "comprising" language in the preceding claims, the instant claims encompass virtually every antibody in existence. Hopp et al. disclose a monoclonal antibody that meets the limitations of the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 95 and 96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Isenberg et al. (Neuroreport, 1993, 5, pp.121-124).

Claims 95 and 96 encompass an antibody which binds to an epitope on a polypeptide comprising an amino acid sequence homologous to SEQ ID NO: 105. Isenberg et al. disclose an amino acid sequence of a fragment of a 5HT3 receptor. The amino acid sequence of Isenberg et al. comprises an epitope of eight consequent amino acids, which completely match an epitope of SEQ ID NO: 105, see a copy of an alignment printout attached to the instant office action. Therefore, an antibody which binds to an epitope of a fragment of 5HT3 receptor of Isenberg et al. would anticipate the instant claims.

Isenberg et al. do not expressly disclose an antibody to a fragment of 5HT3 receptor. At the time the invention was made it would have been *prima facie* obvious to one of ordinary skill in the art to generate antibodies to 5HT3 receptor for purposes of tissue printing and localization of 5HT3 receptors. Such antibodies would be encompassed by claims 95 and 96.

Conclusion

12. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 782-9306 for regular communications and (703) 782-9307 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D.
January 24, 2003

JOHN ULM
PRIMARY EXAMINER
GROUP 1800